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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,669	08/16/2001	Masahiro Sakanaka	56238(71526)	4547

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EXAMINER	
KHARE, DEVESH	
ART UNIT	PAPER NUMBER
1623	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/913,669	SAKANAKA ET AL.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-36,38-41,52 and 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-36,38-41,52 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's amendments and remarks filed on 12/05/2006 are acknowledged. Claims 32 and 52 have been amended. Claims 1-31,37 and 42-51 have been cancelled previously.

The following is new rejection(s) necessitated by Applicant's amendment filed on 12/05/2006.

An action on the merits of claims 32-36,38-41,52 and 53 is contained herein below.

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 32-36, 38-41, 52 and 53 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 108,119,120 and 121 of co-pending Application No. 10/070209.

Although the conflicting claims are not identical, they are not patentably distinct from each other. The co-pending application claims a method of treating injured nervous tissue such as brain infarction, a cerebral infarction or cerebral apoplexy in a mammal comprising administration of a therapeutic agent ginsenosides Rb_1 or salts thereof in dosages between 1.67 pg/kg/day and 1.67 mg/kg/day wherein said agent is encompassed by or has substantial overlap with the agent of the instant method. All the methods are drawn to methods of treating a mammal or patient suffering from injured nervous tissue. However, the instant method is a method of treating a patient suffering from a traumatic or compression injury of a nervous tissue by administering to a patient a therapeutically effective amount of a pharmaceutical composition comprising a therapeutic agent selected from ginsenosides Rb_1 or its salts between the dosages of 0.000167 mg/kg/day and 1.67 mg/kg/day, which is the underlying mechanism by which the methods of the issued claims are accomplished. It would have been obvious to one having ordinary skill in this art, at the time the claimed invention was made to select ginsenosides Rb_1 or salts thereof set forth in the claims of the co-pending application and administer them for the claimed method. In doing so, the present method would be achieved. It would be within the scope of the artisan in this art to use ginsenoside Rb_1 in treating a patient suffering from the traumatic or compression injuries to the nervous

tissue due to their inherent properties of ginsenoside Rb_1 in the treatment of the injured nervous tissue.

The examiner notes the instant claims and said co-pending applications of applicants do indeed substantially overlap therefore this obviousness-type double patenting rejection is necessary to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees.

These are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

Claims 32-36, 38-41, 52 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakanaka et al. (Sakanaka) (Jpn. J. Pharmacol. 67, Suppl. I, 297 P,1995) in combination with Liu (U.S. Patent 4,708,949) in view of Zhang et al. (Zhang) (Acta Pharmacologica Sinica 17(1), 44-48, 1996 Jan.) in combination with Lim et al. (Neuroscience Research, 28, 191-200,1997).

Sakanaka teaches red ginseng powder containing ginseng saponins and ginsenoside Rb_1 prevented "ischemia-induced learning disability and rescued ischemic hippocampus CA1 neurons in gerbils (see Abstract, P 297).

While the Sakanaka teaches that ginsenoside Rb_1 is one of the neuroprotective molecules within ginseng root, which can be administered by intraperitoneal injections, Sakanaka differs from applicant's method in that Sakanaka does not suggest the effective concentrations of ginsenoside Rb_1.

Liu teaches in abstract the therapeutic compositions composed of four plant extracts: ginsenoside, tetramethyl pyrazine, astragalan and atractylol. This therapeutic composition is highly effective in treating cerebral vascular diseases (also see claims 1-4). In claims 13-17, Liu teaches the method of treating a patient suffering from cerebrovascular disease and impaired neurofunction with a pharmaceutical composition comprising ginsenoside.

Zhang teaches the influences of ginsenosides Rb_1 and Rg_1 on the brains against ischemia-reperfusion injury (page 44, see AIM). Zhang discloses that ginsenosides such as Rb_1 from Panax ginseng protected rat brains from cerebral infarction (p. 44, 1st para.). Zhang discloses the effects of ginsenoside Rb_1 in rat model when used in the concentration of 10 mg- 40 mg/kg (pp. 46-47, Tables 1-3). Zhang also discloses the effects of Rb_1 on neurologic deficit in rats (Table 1 on page 46). Zhang discloses "Rb_1 can reduce intracellular calcium while the calcium entry into cells is the final common pathway leading to cell death" (page 45, lst col. lst para.).

Lim et al. teach ginsenoside Rb_1 as a neuroprotective agent in the prevention of cerebrovascular diseases (see abstract). Kim et al. disclose a saline containing ginsenoside Rb1 (page 192, 2nd col.,3rd para., lines 6-7). Lim et al discloses that 60 or 600 ng/day ginsenoside Rb_1 infusion to ischemic gerbils (page 192, col.2, Experiment 1). Lim et al. also discloses that infusion of ginsenoside Rb_1 at a dose of 6 μg/day was ineffective in preventing ischemia-induced neuronal damage in gerbils (page 195, col.1, 1st para.). Furthermore, Lim et al discloses that ginsenoside Rb_1 at concentrations of 0.1-100 fg/ml rescued hippocampal neurons from lethal oxidative injury caused by the hydroxyl radical-promoting agent $FeSO_4$ (page 197, col.1, 2nd para.). Lim et al. discloses, "relatively high concentrations of ginsenoside Rb_1 infused into the cerebral ventricles did not protect hippocampal CAI neurons against ischemic injuries in the present study and they occasionally exhibited a neurotoxic rather that neuroprotective effect on ischemic gerbils (page 197, col.2, 2nd para.).

With regard to the very broad ranges of the traumatic or compression injuries to the nervous tissue of claim 52, it would be within the scope of the artisan in this art to use ginsenoside Rb_1 in treating a patient suffering from the traumatic or compression injuries to the nervous tissue due to their inherent properties of ginsenoside Rb_1 in the treatment of the injured nervous tissue. Similarly, the amelioration of paralysis or paraplegia; suppression of secondary degeneration caused by demyelination; and the suppression of apoptosis or apoptosis-like cell death of oligodendrocytes; caused by the nervous tissue injuries can be treated with ginsenoside Rb_1 as obvious to one skilled in this art.

It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller,* 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). See MPEP 2144.05 part II A. Variance of dosage amounts with regard to known pharmaceutically active ingredients was well known in the art. One of ordinary skill in the art would have been motivated to modify the dosage amounts of ginsenoside Rb_1 in order to enable the treatment protocol to be matched with the demands and needs of individuals who needed treatment. Such variations are considered optimization of results effective variables, conventional practice in the art of pharmacology.

Therefore, one of ordinary skill in the art would have found the applicants claimed method of treating a patient suffering from a traumatic or compression injury of a nervous tissue by administering to said patient a therapeutically effective amount of a pharmaceutical composition comprising a therapeutic agent selected from ginsenoside Rb_1 to have been obvious at the time the invention was made having the above references before him because Sakanaka and Liu teach that ginsenoside Rb_1 from plant source is to prevent "ischemia-induced learning disability and rescued ischemic hippocampus CA1 neurons in gerbils" and of treating a patient suffering from cerebrovascular disease; and Zhang and Lim et al. teaches effective concentrations of ginsenoside Rb_1 in protecting rat brains from cerebral infarction. The motivation for using lower concentrations of ginsenoside Rb_1 is provided by Lim et al, which suggests

"relatively high concentrations of ginsenoside Rb_1 infused into the cerebral ventricles did not protect hippocampal CAI neurons against ischemic injuries in the present study and they occasionally exhibited a neurotoxic rather that neuroprotective effect on ischemic gerbils (page 197, col.2, 2nd para.).

Response to Arguments

Applicant's remarks filed on 12/05/2006 traversing the rejections of claims 32-36, 38-41, 52 and 53 under 35 U.S.C. 103(a) have been fully considered but they are not persuasive.

It is noted that Sakanaka abstract is fully disclosed in the Wen reference, which was provided by the applicant on 04/10/2006.

Applicants argue, "Sakanaka in combination with Liu and Zhang, does not provide all of the claim limitations of Applicant's claim 32, as Zhang does not provide for a dosage range of ginsenoside Rb_1 of 0.000167 (0.167 fg) mg/kg/day to 1.67 mg/kg/day."

It would be within the scope of the artisan in this art to use ginsenoside Rb_1 in treating a patient suffering from the traumatic or compression injuries to the nervous tissue due to their inherent properties of ginsenoside Rb_1 in the treatment of brain ischemia as set forth by Sakanaka and Zhang references. Furthermore, Lim et al. discloses, "relatively high concentrations of ginsenoside Rb_1 infused into the cerebral ventricles did not protect hippocampal CAI neurons against ischemic injuries in the present study and they occasionally exhibited a neurotoxic rather that neuroprotective effect on ischemic gerbils (page 197, col.2, 2nd para.). Lim et al discloses that ginsenoside Rb_1 at

concentrations of 0.1-100 fg/ml rescued hippocampal neurons from lethal oxidative injury caused by the hydroxyl radical-promoting agent $FeSO_4$ (page 197, col.1, 2nd para.).

Indeed, the examiner has established a prima facie case of obviousness rendering claims 32-36, 38-41, 52 and 53 rejected under 35 U.S.C. 103(a) by addressing sufficiently all of the limitations set forth in the instant claims for a method of treating a patient suffering from a traumatic or compression injury of a nervous tissue comprising administering to a patient therapeutically effective amount of a pharmaceutical composition comprising a dosage range of ginsenoside Rb_1 of 0.000167 (0.167 fg) mg/kg/day to 1.67 mg/kg/day, one skilled in the art would have a reasonable expectation for success in combining the teachings of Sakanaka; Liu; Zhang and Lim et al. references to accomplish said method.

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (571)272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang, Supervisory Patent Examiner, Art Unit 1623 can be reached at

(571)272-0627. The official fax phone numbers for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Devesh Khare, Ph.D.,J.D.
Art Unit 1623

January 3, 2007